

### ABSTRACT

The invention features a waveguide based devices, methods, and systems to increase sensitivity of surface plasmon resonance (SPR) measurement through the use of differential detection. The enhanced sensitivity enables analysis and detection of a wide range of analytes including, for example, DNA, antibodies, proteins, and other chemical compounds. These methods achieve this result by sampling the SPR response curve at more than one point. This can be achieved using a detection device with sets of optical waveguides having distinct propagation parameters, or by using light of different wavelengths. These methods are suitable for multi-analyte and multi-sample applications in a miniaturized detection system. Furthermore, this invention makes use of an alternating polarity electric field to reduce nonspecific analyte binding and detection time.

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